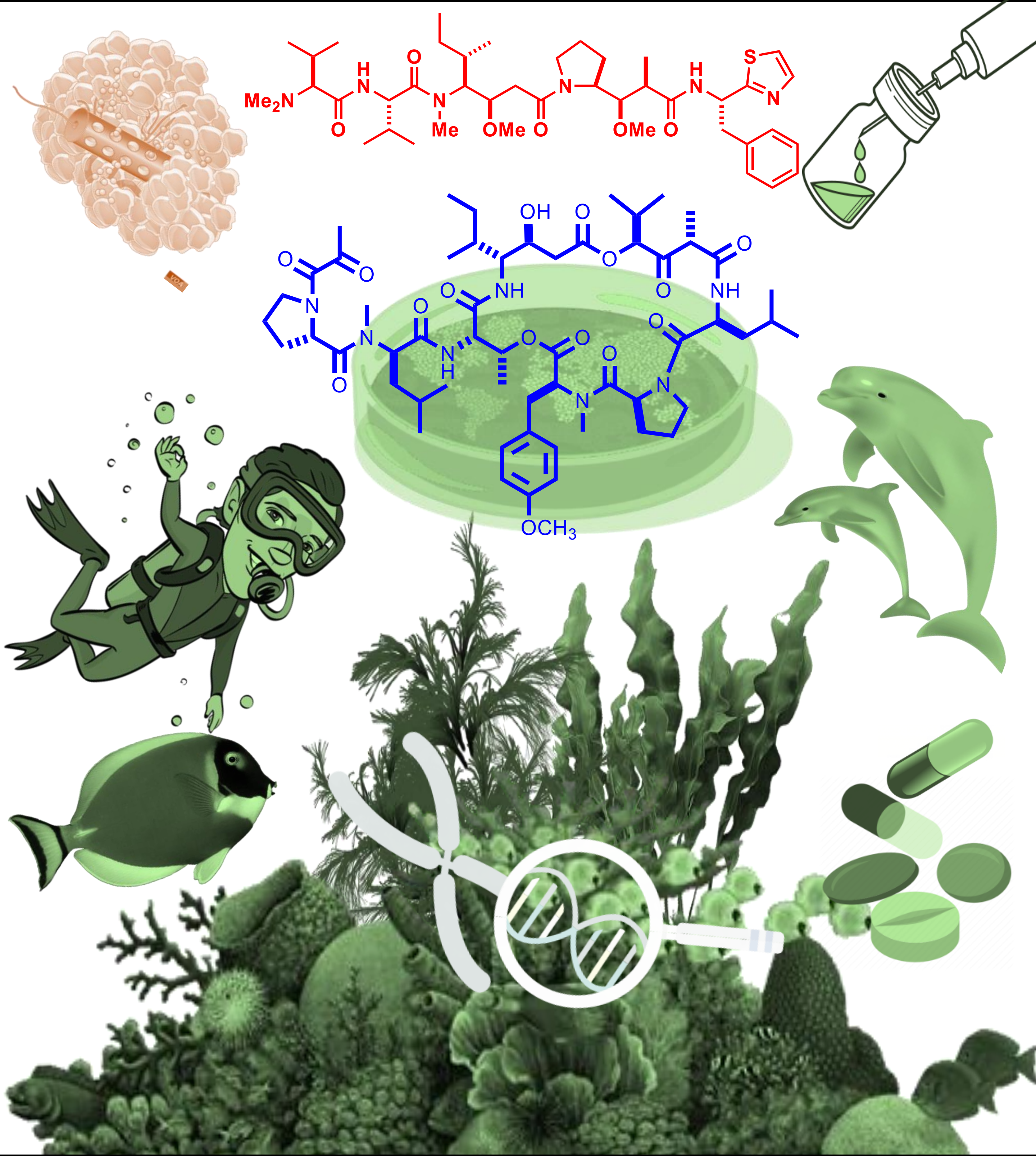
Marine Drugs

2021 – 2022 {Lecture 5}



Dr. Omar M. Sabry

Marine Drugs

III. Marine Pharmaceuticals {Approved Marine Drugs}

1. Cytarabine - Ara C - Cytosar-U®

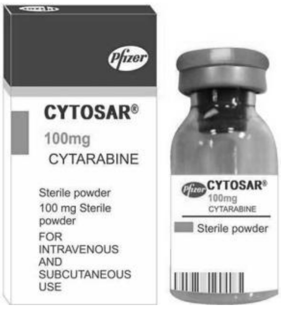
Name: Cytarabine - Ara C - CytosarR

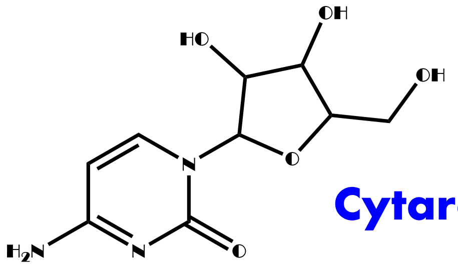
Nature: Nucleoside {Arabinosyl cytosine}

Source: Caribbean marine sponge *Cryptotethya crypta*

Mechanism of action: Anti-metabolite that inhibits DNA polymerase

Medical uses: Acute myelocytic leukemia





Cytarabine

2. Vidarabine - Ara A®

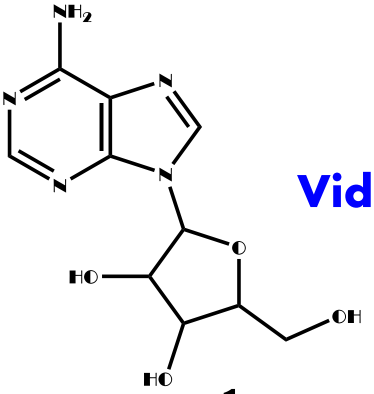
Name: Vidarabine

Nature: Nucleoside {Arabinosyl adenine}

Source: *Streptomyces antibioticus* {used as antiviral}

Mechanism of action: Anti-metabolite inhibits DNA polymerase

Medical uses: Herpes simplex virus and Varicella zoster {Chickenpox virus}.



Vidarabine - Ara A

3. Plitidepsin® - Aplidin®

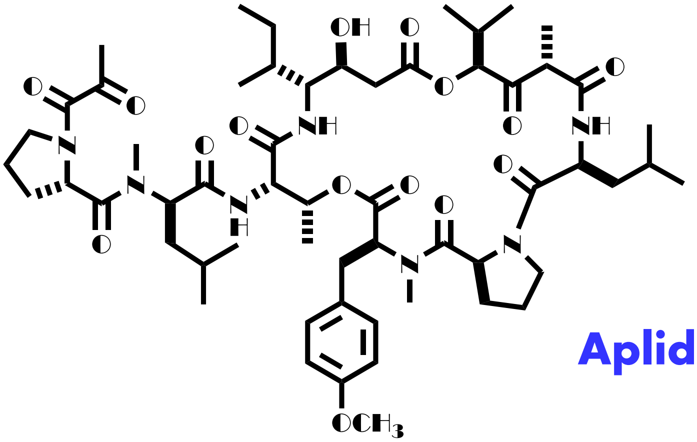
Name: Plitidepsin - Aplidin®

Nature: Cyclic depsipeptide

Source: Tunicate *Aplidium albicans* {Now it is totally synthetic}

Mechanism of action: Induction of apoptosis.

Medical uses: Used in Multiple myeloma and Pancreatic cancer



Aplidin

4. Eribulin – Halaven®

Name: Eribulin – Halaven

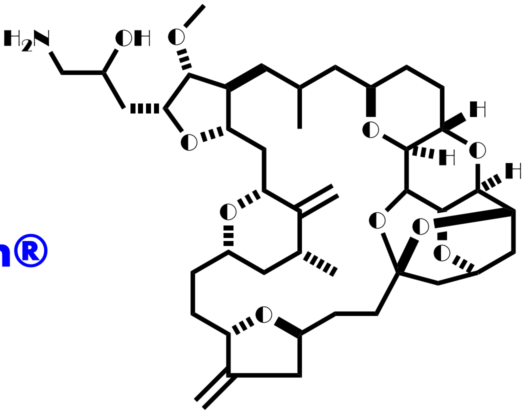
Nature: Macrocyclic polyether {Polyketide}

Source: Synthetic compound inspired from Halichondrin B {from *Halichondria* sponge}.

Mechanism of action: Microtubule destabilization {Stop mitosis}.

Medical uses: Breast cancer – Liposarcoma

Eribulin - Halaven®



Structural trimming:

It is the removal of certain part of the bioactive compound during chemical synthesis to decrease side effects, increase selectivity, decrease toxicity or increase bioavailability e.g. Structural trimming of Halichondrin B was carried out to obtain Eribulin.

5. Ziconotide {Prialt®}

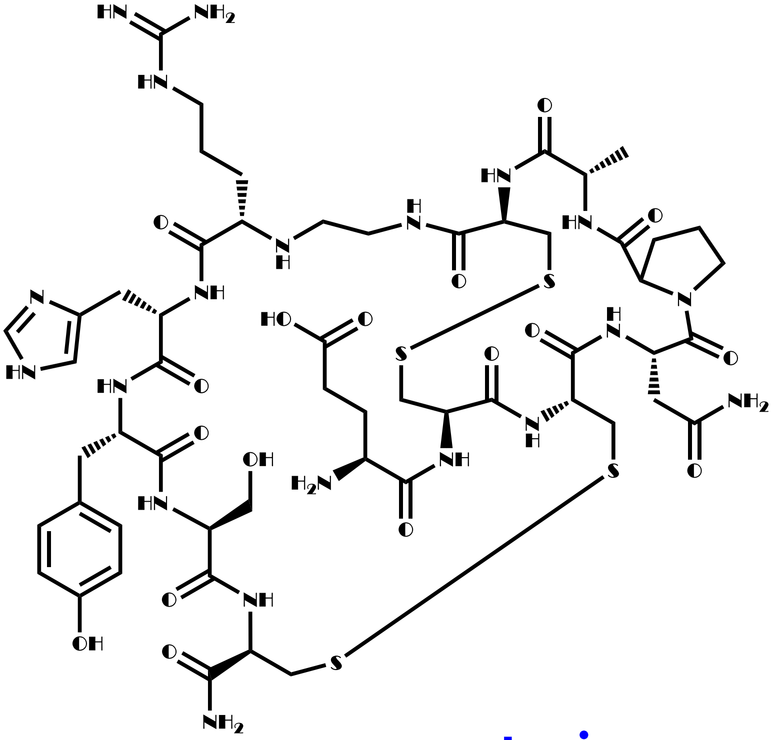
Name: Ziconotide {Prialt®}

Nature: Cyclic polypeptide 25 amino acids inspired from ω-conotoxin

Source: Cone snail {Conus magus}.

Mechanism: Acts as a Ca++ Channel blocker in the neurons of the spinal cord.

Medical uses: Strong analgesic in cancer and fractures. must be injected Intrathecal {Directly in the spinal cord} to prevent any loss of the compound in other body organs and to prevent its hydrolysis.



ω-conotoxin

Story of Ziconotide {Prialt®}

A snail called *Conus magus* in Philippine attacks fish by injecting mixture of cyclic peptides into fish {more than 100 polypeptides}, paralyzing them then predate on them. The major bioactive polypeptide found in cone snail venom was ω-conotoxin {27 amino acids polypeptide} which block voltage-gated calcium channels in neurons. The synthetic analogue of ω-conotoxin {Ziconotide - Prialt® 25 amino acids polypeptide} was produced and marketed now in year 2004. It is used to treat severe chronic pain in people who cannot use or do not respond to standard pain-relieving medications.

6. Brentuximab {ADCETRIS®}

Name: Brentuximab

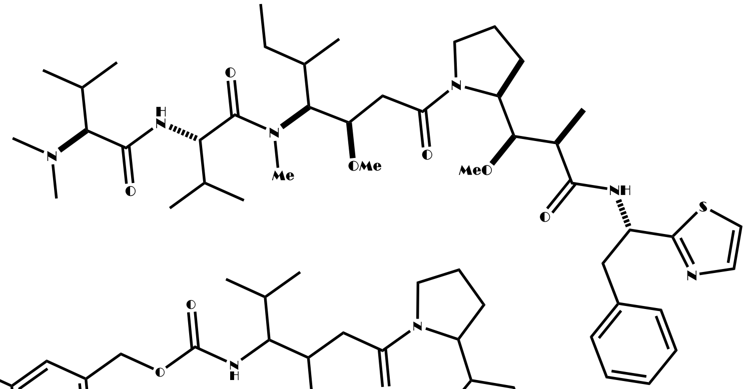
Nature: Polypeptide monoclonal antibody conjugate

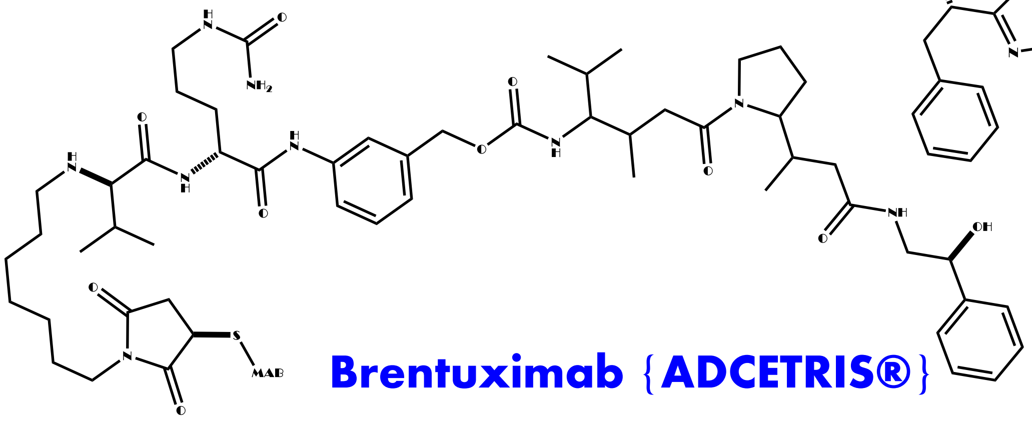
Source: Synthetic conjugate inspired from dolastatin 10

Mechanism: Microtubules stabilizer {anti-mitotic}

Medical uses: Lymphoma.

Dolastatin 10





Brentuximab {ADCETRIS®}